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Alexandria, VA 22313-1450

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Gauldie, *et al.*

Attorney Docket No: ARK-P001

Application No: 09/742,892

Art Unit: 1635

Filed: 12/21/2000

Examiner: Schnizer, Richard A.

For: ACNE VACCINE

TRANSMITTAL OF APPEAL BRIEF
(PATENT APPLCIATION – 37 C.F.R. § 1.192)

1. TRANSMITTED DOCUMENTS: the following documents relating to the above-identified patent application are being transmitted herewith.

_X_ a. An Appeal Brief, in triplicate for this application: _16_ pages, in response to the Petition for Revival granted on 04/23/2004;

_X_ b. An Amendment for this application: _7_ pages, in relation to the Petition for Revival granted on 04/23/2004;

_X_ c. A stamped, self-addressed, return postcard; and

_X_ d. A Check (# _1071_) for $ _165.00_ to cover required fees of this correspondence.

2. STATUS OF APPLICANT

This application is on behalf of

[ ] other than a small entity

[x] small entity

A statement:

[ ] is attached.

[x] was already filed.

3. FEE FOR FILING APPEAL BRIEF

Pursuant to 37 C.F.R. 1.17 (c), the fee for filing the Appeal Brief is:

[x] small entity

$165.00

[ ] other than a small entity

$320.00

Pursuant to 37 C.F.R. 1.17 (d), the fee for request for Oral Hearing is:

[ ] small entity

$140.00

[ ] other than a small entity

$280.00

Appeal Brief fee due $ 165.00

4. EXTENSION OF TERM

The proceedings herein are for a patent application and the provisions of 37 C.F.R. §1.136 apply.

(a) [ ] Applicant petitions for an extension of time under 37 C.F.R. §1.136 (fees: 37 C.F.R. § 1.17 (a) (1)-(5)) for the total number of months checked below:

	Extension (months)	Fee for other than small entity	Fee for small entity
[ ]	one month	$110.00	$55.00
[ ]	two months	$410.00	$205.00
[ ]	three months	$930.00	$465.00
[ ]	four months	$1,450.00	$725.00
[ ]	five months	$1,970.00	$985.00

Fee: $_____

If an additional extension of time is required, please consider this petition thereof.

[ ] An extension for _____ months has already been secured, and the fee paid therefore of $ _____ is deducted from the total fee due for the total months of extension is now requested.

Extension fee due with this request $ _____

or

(b) [x] Applicant believes that no extension of term is required. However, this conditional petition is being made to provide for the possibility that applicant has inadvertently overlooked the need for a petition and fee for extension of time.

5. TOTAL FEE DUE

The total fee due is:

Appeal Brief Fee $ 165.00

Extension Fee (if any) $ _____.

6. FEE PAYMENT

[x] Attached is check No. 1071 in the sum of $ 165.00. However, in case Applicant inadvertently miscalculated any required fee, the Commissioner is hereby authorized to charge the necessary additional amount associated with this communication or credit any overpayment to **Deposit Account No. 500482.** A duplicate copy of this authorization is enclosed.

[ ] Charge Account No. **500482** the sum of $ _____.
A duplicate of this transmittal is attached.

7. FEE DEFICIENCY

[x] If any additional extension and/or fee is required, this is a request therefore and to charge Account No. 500482.

AND/OR

[ ] If any additional fee for claims is required, charge Account No. _____.

Respectfully submitted,

6/23/2004
Date

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor:	GAULDIE, *et al.*	Attorney Docket No.:	ARK-P001
Serial No.:	09/742,892	Group Art Unit:	1635
Filed:	December 21, 2000	Examiner:	Schnizer, Richard A.
Title:	ACNE VACCINE		

BRIEF ON APPEAL

Mail Stop Appeal Brief-Patents
Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The following appeal brief is submitted pursuant to the appeal filed March 8, 2004 in the above-identified application.

REAL PARTY IN INTEREST

The subject application is owned by Arkagen, Inc. of California.

STATUS OF CLAIMS

Claims 1, 4-14, 17-19, and 21-25 stand under final rejection, from which rejection this appeal is taken.

STATUS OF AMENDMENTS

The Appellants filed an amendment in response to the Final Rejection. In an Office action mailed December 29, 2003 the examiner indicated that the amendment was entered.

The Appellants are filing an amendment making a revision to claims 1 and 11 concurrently with this appeal brief to remove issues from appeal. For the reasons explained in the Remarks section of that amendment, Appellants believe that that amendment is entitled to entry under the standards set forth in MPEP §1207.

SUMMARY OF INVENTION

Appellants' invention as presently claimed is directed to compositions and methods useful for eliciting immunity directed towards *Propionbacterium acnes.* The claims on appeal are set forth in Appendix A. Claims 1 and 11 are set forth first without the amendment and then with the amendment.

Propionbacterium acnes is a bacterium implicated in the etiology of Acne vulgaris and possibly other pathological states. Appellants' approach to containing *P. acnes*' harmful effects is eliciting an immune response by viral or naked DNA vaccination directed to the exoenzyme lipase of the bacterium. As stated in the patent specification, paragraphs [0005]-[0008], identification of effective immunological targets is especially challenging in this case because the bacterium can live inside macrophages. Anti-lipase genetic immunization draws immunity protective against *P. acnes* in mice as shown in FIG. 2.

ISSUES

Whether claims 1, 4-14, 17-19, and 21-25 are supported by an enabling disclosure in accordance with 35 U.S.C. §112, first paragraph. Whether claims 1, 4-14, 17-19, and 21-25 are supported by a written description in accordance with 35 U.S.C. §112, first

paragraph. Whether claims 1, 7, 10-12, 21, 22, and 24 are patentable under 35 USC §102(b) over Stickl (US Patent 4,057,627).

GROUPING OF CLAIMS

With respect to the enablement rejection, claims 1, 4, 7-14, 17, 21-23 stand or fall together, claims 5, 6, and 18 stand or fall together, claims 19 and 25 stand or fall together, and claim 24 stands or falls by itself. With respect to the written description rejection all claims stand or fall together. With respect to the §102(b) rejection all rejected claims stand or fall together.

ARGUMENT

I. THE ISSUES UNDER 35 U.S.C. §112, FIRST PARAGRAPH, ENABLEMENT REQUIREMENT

The rejection raises the questions of 1) whether the specification needs to enable claims of breadth that encompasses complete inhibition or cure of diseases caused by *Priopionbacterium acnes*, and 2) whether results of genetic vaccinations in mice are indicative of similar results that may be obtained in humans.

Compliance with the enablement clause of 35 U.S.C. §112 requires that the disclosure be sufficiently full, clear, concise and exact to enable an artisan to practice the claimed invention without undue experimentation. The scope of enablement provided by the disclosure must be commensurate with the scope of protection sought by the claims.

Breadth of claims

In the first paragraph of the Advisory Action Examiner states that all claims are considered to be of a broad scope embracing reducing the size of abscesses caused by *P.*

acnes infections, completely inhibiting or curing any disease caused by *P. acnes*, including Acne vulgaris. Appellants argue that the claims are construed too broadly.

The invention as claimed in claims 19 and 25 covers compositions of matter without any recitation of function. While the compositions of matter claimed are useful in eliciting an immune response if administered to a recipient, it is improper to read into these claims very broad functions such as complete and/or permanent cures. Therefore, it is irrelevant with respect to claims 19 and 25 whether the specification does or does not enable broad applications such as complete and/or permanent cures. Claims 19 and 25 are enabled because the specification teaches those of skill in the art how to make and how to use the claimed compositions of matter.

The invention as claimed in claims 1, 4-14, 17, 18, 21-23 is drawn to compositions and methods for treating conditions caused by *P. acnes*. Examiner apparently interpreted the term "treating" as encompassing any conceivable positive outcome of administering the claimed vaccines. Appellants respectfully submit that this interpretation is too broad. The term "treat" in this context refers to giving a subject medical care, not to specific outcomes of the treatment. Administration of the claimed vaccines results in immunity specific to *P. acnes*. It is essentially this result that was intended to be covered by the term "treating". Therefore, to be enabling the specification does not have to teach how to entirely prevent or totally cure any *P. acnes*-related ailment.

Amendments to claims 1 and 11 presented concurrently with this Appeal Brief clarify that the intended use of the vaccines is to generate an immune response in the recipient. Claims 4-10, 12-14, 17, 18, 21-23 depend from either claim 1 or claim 11 and

therefore comprise the same intended use. Because the specification enables generating an immune response in the recipient, claims 1, 4-14, 17, 18, 21-23 as amended are supported by an enabling specification.

The invention as claimed in claim 24 is directed to a method of cosmetically improving the appearance of a person's skin who is suffering from Acne vulgaris using a composition comprising a vector designed to immunize a recipient to *P. acnes*. Acne vulgaris is caused at least in part by *P. acnes*. As explained above and below, the claimed vaccines bring about anti-*P. acnes* protective immunity. Therefore, the specification enables one of skill in the art to cosmetically improve the appearance the skin of a person suffering from Acne vulgaris because specific anti-*P. acnes* immunity aids in clearing or controlling the growth of *P. acnes*.

Results from genetic immunization of mice are indicative of similar responses in humans

Part of the enablement rejection is based on Examiner's finding that mice or other animal test results of DNA vaccines cannot be extrapolated to humans. This finding is based mainly on McCluskie et al., Molecular Medicine 5: 287-300, 1999 (hereinafter "McCluskie"). Examiner has the initial burden of establishing a reasonable basis to question the enablement provided in the claimed invention explaining why he believes the subject matter of the claims is not enabled. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

In response to Examiner's reliance on McCluskie Appellants have pointed out a many flaws in the reference (*see* Appellants' Response to the Final Action, pages 12-13). Because the reference is unreliable the Examiner failed to meet his burden of explaining why the claims are not enabled. Additionally, Appellants have presented evidence

contradicting McCluskie's view that mice are not relevant for DNA vaccines (*see* Appellants' Response to the Final Action, page 14). Moreover, McCluskie only addresses DNA vaccines, while some claims in the application are directed exclusively to viral based vaccines (*see* Appellants' Response to the Final Action, page 12); for these claims, McCluskie simply cannot be relevant. Thus, Examiner's reliance on McCluskie is misplaced, and therefore the results of mice experiments as shown in the specification enable those of skill in the art to practice the invention without undue experimentation.

McCluskie presents a small-scale research study of naked DNA vaccines administered to mice and primates by different routes. The immunization results generally show variability of response between species and routes of administration. In explaining his reliance on this reference for supporting the rejection, Examiner referred in part to the data presented by McCluskie, and in part to general statements in the reference regarding the art.

The data presented in McCluskie is of dubious scientific value. In fact, the authors of the reference themselves point out that the disproportionately large injection quantities used in mice for immunization cannot be directly compared to amounts used in humans or primates. Regarding immunization success using different routes of administration Appellants pointed out that McCluskie did not even attempt to optimize common variables (*see* Appellants' Response to the Final Action, pages 15).

The vast difference between the amounts of vaccines administered to mice and primates or humans strongly questions Examiner's conclusion that mice are irrelevant animal models for the development of DNA vaccines for humans. Nevertheless, in the Advisory Action, the Examiner states that it is Appellants' duty to prove that mice and

human results are comparable when proportional amounts of the vaccine are used. This is not so because, as stated above, the Examiner has the burden of proving that Appellants' disclosure is not enabling. Because the Examiner relied on flawed data to support his conclusion, he did not meet his burden of proof for an enablement rejection, and therefore the rejection must be withdrawn.

Nevertheless, Appellants have presented evidence that animal models have been used in the development of DNA vaccines by those of skill in the art with the expectation that similar human therapies. Thus, those of skill in the art did not share McCluskie's view, as adopted by the Examiner, that animal results are not indicative of similar human responses to DNA vaccines. In the Response to the Final Action on page 14, Appellants pointed to Gerdts et al. and Tacket et al. to show that workers in the field of DNA vaccines essentially ignored the views of McCluskie. In the Advisory Action the Examiner did not refer to these references at all. In addition to those, Appellants can also point, for example, to US Patent Nos. 6,696,421, 6,284,533, 6,451,769, which disclose studies of DNA vaccines in mice for developing human therapies. McCluskie's warnings have been disregarded by those of skill in the art, implicitly questioning their value.

In addition to the data presented in McCluskie the Examiner bases the enablement rejection on a few general statements from McCluskie regarding DNA vaccines. In the Advisory Action Examiner refers to McCluskie as presenting "a balanced view of the art" (second paragraph), while Appellants have pointed to the reference's bias as it attempts to justify the study presented (), not to objectively review the art. For example, Examiner quoted approvingly McCluskie's speculation (which is apparently called "reasonable explanation" in the Advisory Action) that it is differences in transfection and

expression efficiencies of antigens encoded by DNA vaccines make non-primate models inappropriate for development of human vaccines. In response to this, Appellants pointed to the 504 human clinical trials that are based on transfection and expression of foreign genes to prove that those of skill in the art consider transfection and expression of foreign genes in humans feasible. In the Advisory Action Examiner apparently indicates that this evidence does not address an issue, which implicitly means that McCluskie's credibility is not an issue. Actually, as explained above, McCluskie's credibility is an issue because it is Examiner's duty to prove that the disclosure is non-enabling, and proof should be supported by trustworthy reasoning.

Claims 5, 6, and 18 are drawn to virus-mediated immunization, not naked DNA vaccines. Claim 25 is similar to claims 5, 6, and 18 in this respect. McCluskie, on the other hand, deals only with DNA vaccines. Appellants have argued therefore that McCluskie cannot support the rejection of claims 5, 6, and 18 (*see* Appellants' Response to the Final Action, pages 15). In the Advisory Action Examiner finds this "...unpersuasive because claims 1, 7-14, 19, and 21-24 are not limited to a viral vector and clearly encompass naked DNA vaccines". Examiner's finding is puzzling as Appellants clearly stated they were referring only to claims 5, 6, and 18. Then, Examiner states that Appellants provided no evidence or reason to expect that McCluskie would not hold true for virus-mediated vaccines as well. Again, Appellants do not have to provide any reasons or evidence with respect to these claims because Examiner quite clearly failed to meet his burden of reasonably questioning the enablement of claims 5, 6, and 18. Moreover, in explaining that the results of McCluskie do not support its conclusions,

applicants implicitly provided an excellent reason for expecting that the results would not hold true for virus mediated vaccines.

In addition to relying on McCluskie, Examiner questions enablement of the claims based on a finding that the mouse is not a widely accepted animal model for Acne vulgaris. Appellants have addressed Examiner's concerns on pages 16-18 of the Response to the Final Action. Examiner replied in the fourth paragraph of the Advisory Action that "Applicant has presented no evidence that the results can be extrapolated, i.e. that the model used is an accepted animal model, or that the differences between mouse and human physiology are insignificant in the context of the invention ...". Because this reply is outright unresponsive to the text on pages 16-18, Appellants cannot add anything to their explanation provided in the Response to the Final Action. However, it is worth noting that the "breadth of claims" section above also explains why the mouse needs only be a model of immune response to a vaccine, not a model of Acne vulgaris. In addition, the amendments proposed at the time of submission of this appeal brief would make it clearer that the mouse need not be a model of Acne vulgaris as the claims (other than claim 24) are only drawn to compositions and methods for generating an immune response.

The Advisory Action contains a statement that the claims lack enablement for the reasons of record. However, the amendments presented in response to the final rejection and entered made many of the reasons of record inapplicable to the amended claims. The arguments presented above explain why Examiner's rejection as it applies to the amended claims should be withdrawn. Re-consideration of the *ex-parte* Forman factors as applied

to the claims as amended, in light of the evidence and arguments presented by Appellants, should support the conclusion that the claims are enabled.

II. THE ISSUES UNDER 35 U.S.C. §112, FIRST PARAGRAPH, WRITTEN DESCRIPTION REQUIREMENT

In the Advisory Action Examiner indicates that all claims are rejected as non-compliant with 35 U.S.C. §112, first paragraph, written description requirement. Examiner explains that the claims are drawn to a genus of nucleic acids *P. acnes* lipase and fragments thereof, and therefore embrace any naturally existing or recombinantly produced variant of a lipase derived from *P. acnes*. Then, the Examiner goes on to state that the specification as filed discloses none of these variants or their fragments.

To comply with 35 U.S.C. §112, first paragraph, written description requirement, the specification must convey to those of skill in the art that Appellants at the time the application was filed were in possession of the invention as claimed.

The specification discloses actual reduction to practice of nucleic acids encoding the *P. acnes* lipase, but does not reproduce the amino acid sequence of the protein that was previously reported. Designation of a gene as "*P. acnes* lipase" is sufficient for those of skill in the art to communicate the actual sequence of the protein because the sequence is reported in the literature and is immediately accessible. To date there is no indication of any naturally occurring variants of the polypeptide. Common features and attributes of the members of the genus is their derivation from the *P. acnes* lipase sequence and their immunogenicity when used as polypeptide antigens. Use of polypeptides as immunogens is a mature art, and making of immunogenic fragments

from a full-length sequence can be routinely achieved by conventional methods such as molecular biology. Therefore, reference to the known full length *P. acnes* lipase is sufficient to describe a representative species, which is sufficient to describe the genus because those of skill in the art would recognize that Appellants were in possession of the necessary common attributes or features possessed by the members of the genus.

Consequently, within the context of the present claims, "*P. acnes* lipase or fragment thereof" is compliant with the written description requirement because those of skill in the art can recognize that Appellants were in possession of the genus of immunogenic molecules at the time of filing of the application.

III. THE ISSUES UNDER 35 U.S.C. §102(b)

Claims 1, 7, 10-12, 21, 22, and 24 were rejected under 35 U.S.C. §102(b) as being anticipated by Stickl (US Patent 4,057,627). Stickl discloses use of a composition of attenuated *P. acnes* as oral vaccines.

In response to this rejection Appellants argued that all claims are limited by the term "vector", which is defined in the specification as a "genetically engineered nucleic acid construct". In the last paragraph of the Advisory Action Examiner responds that nucleic acids in Stickl are "... products of natural selection, and as such have been genetically engineered through mutation and recombination".

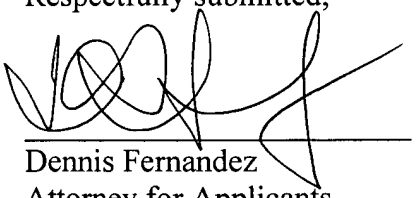
Appellants respectfully submit that Examiner's interpretation of "genetic engineering" is too broad, thus rendering the term meaningless. If all products of natural selection are genetically engineered, then all living matter is a product of genetic engineering. There are several definitions of genetic engineering, and they generally

involve use of modern molecular biological techniques to alter genetic material. Consistent with this definition, Appellants disclosed vectors such as naked DNA or recombinant viral vectors. In perhaps the broadest definition, genetic engineering includes selective breeding or artificial selection. Even according to this definition, the compositions disclosed in Stickl do not comprise a vector as defined by Appellants. There is no indication in Stickl that the strains *P. acnes* used were genetically manipulated in any way. Because Stickl does not use a vector within the meaning of the claims it does not anticipate the claims under 35 U.S.C. 102(b).

CONCLUSION

For the reasons advanced above, Appellants respectfully urge that the rejections of the claims are improper. Reversal of the rejections in this appeal is respectfully requested.

Respectfully submitted,



Date: 6/23/2004

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APPENDIX

1. A vaccine useful in treating diseases caused by *Propionibacterium acnes*, said vaccine comprising at least one vector that comprises at least one nucleotide sequence encoding a lipase or fragment thereof derived from said *Propionibacterium acnes*, and wherein said lipase or fragment thereof is capable of generating an immune response in a recipient thereof.

1. (as amended) A vaccine useful to generate an immune response to a lipase of *Propionibacterium acnes* in a recipient thereof, said vaccine comprising at least one vector that comprises at least one nucleotide sequence encoding said lipase or fragment thereof derived from said *Propionibacterium acnes*.

4. The vaccine of claim 1, wherein said vector comprises naked DNA, a recombinant viral vector, or a combination of both.

5. The vaccine of claim 1, wherein said vector is selected from the group consisting of adenovirus, adeno-associated virus, herpes virus, vaccinia and RNA viruses.

6. The vaccine of claim 5, wherein said vector is an adenovirus.

7. The vaccine of claim 1, wherein said vector further comprises a nucleotide sequence encoding an adjuvant.

8. The vaccine of claim 7, wherein said adjuvant is a cytokine.

9. The vaccine of claim 8, wherein said cytokine is IL-2, IL-12, or both.

10. The vaccine of claim 1, wherein said nucleotide sequence encodes said lipase.

11. A method of treating a disease caused by *Propionibacterium acnes*, said method comprising obtaining a vaccine comprising at least one vector that comprises at least one nucleotide sequence encoding a lipase or fragment thereof derived from said *Propionibacterium acnes*; and administering said vaccine to a recipient in need thereof.

11. (as amended) A method of generating an immune response in a recipient, said method comprising obtaining a vaccine comprising at least one vector that comprises at least one nucleotide sequence encoding a lipase or fragment thereof derived from said *Propionibacterium acnes*; and administering said vaccine to a recipient in need thereof.

12. The method of claim 11, wherein said administering comprises routes of administration comprising oral, intravenous, intramuscular, transcutaneous, subcutaneous, aerosol, intraperitoneal, or combinations thereof.

13. The method of claim 12, wherein administering comprises transcutaneous administration.

14. The method of claim 13, wherein said transcutaneous administration comprises applying said at least one vector to a patch, and adhering said patch to skin of said recipient.

17. The method of claim 11, wherein said at least one vector comprises naked DNA, a recombinant viral vector, or a combination of both.

18. The method of claim 11, wherein said vector is an adenovirus.

19. A kit comprising a container and one or more patches, wherein said patches have disposed thereon at least one vector comprising a nucleotide sequence encoding a lipase or fragment thereof derived from *Propionibacterium acnes*.

21. The vaccine of claim 1, wherein said vaccine is in the form of an aqueous solution.

22. The vaccine of claim 1, wherein said vaccine further comprises a nucleotide sequence encoding a co-stimulatory molecule.

23. The vaccine of claim 22, wherein said co-stimulatory molecule comprises a B7 protein, a CD40 protein, or both.

24. A method of cosmetically improving the appearance of a person's skin who is suffering from acnes vulgaris, said method comprising the steps of obtaining a composition comprising a mixture of at least one vector that comprises at least one nucleotide sequence encoding a lipase or fragment thereof derived form *P. acnes*, and a cosmetic agent; and administering said composition to said person.

25. A composition comprising an adenovirus vector that comprises a nucleotide sequence encoding a lipase derived from *Propionibacterium acnes*.